

## BEST AVAILABLE COPY

APPLICANT(S): GAZIT, Dan et al.  
SERIAL NO.: 10/067,980  
FILED: February 8, 2002  
Page 6

P-4891-US1

### REMARKS

Claims 1-63 are pending in the application. Claims 23-29 and 42-47 have been rejected. Claims 1-22, 25, 44, and 48-63 have been cancelled. Claims 23-29 and 42-47 have been amended. Amendments to the claims contain no new matter. Therefore, Applicants respectfully request entry of the Amendment.

### OATH/DECLARATION

In the Office Action, the Examiner objected to the Oath/Declaration because the absence of signatures by all other inventors except Stefan Czichos in the Oath/Declaration submitted in the Response to Notice to File Missing Parts submitted by Applicants on June 11, 2003.

Applicants respectfully draw the Examiner's attention to the Oath/Declaration submitted in the Response to Notice to File Missing Parts submitted by Applicants on November 18, 2002, in which two complete Declaration and Power of Attorney forms, containing the signatures of all inventors except Stefan Czichos, were submitted. For your convenience, we attach hereto as Exhibit A the Declaration and Power of Attorney forms submitted on November 18, 2002, including the post-card evidencing filing. Accordingly, Applicants maintain that the requirements for an Oath/Declaration have been fulfilled, and thus request that the Examiner withdraw the objection.

### SEQUENCE COMPLIANCE

The Examiner has objected to the subject specification as containing nucleotide sequences that have not been assigned SEQ ID NOs.

In response, Applicants submit herewith a copy of the following:

1. an initial computer readable for (CRF) copy of the Sequence Listing;

Confidential

# BEST AVAILABLE COPY

APPLICANT(S): GAZIT, Dan et al.  
SERIAL NO.: 10/067,980  
FILED: February 8, 2002  
Page 7

P-4891-US1

2. an initial paper copy of the Sequence Listing, as well as this Amendment directing its entry into the subject specification; and

3. a statement that the content of the paper and computer readable copies are the same and where applicable include no new matter as required.

In view of the foregoing, the subject Application is in compliance with the requirements of 37 CFR 1.821 through 1.825. Accordingly, Applicants respectfully request that the Examiner withdraw the objection.

## PRIORITY REJECTIONS

The Examiner objected to Applicants' claim to priority for the pending and examined claims of the subject application from U.S. Patent Application 09/376,276, filed August 18, 1999, which claims foreign priority of the German Patent Application No. 198.37.438.0, filed August 18, 1998, alleging that "the method of repairing or forming a cartilage in a subject in need and the composition as claimed are not supported by the specifications" of the parent applications, and therefore the pending and examined claims are only entitled to the priority benefit of the filing date of the subject application, February 8, 2002.

Applicants maintain that the current claims are described and enabled in the parent applications of the subject application, U.S. Patent Application 09/376,276 and German Patent Application No. 198.37.438.0, attached hereto as Exhibits B and C. These parent applications disclose and demonstrate mesenchymal stem cells that express Brachyury protein and their use in formation of bone- and cartilage-forming cells (see page 3, lines 1-3 of U.S. Patent Application 09/376,276 and page 3, fifth paragraph of German Patent Application No. 198.37.438.0). Accordingly, Applicants respectfully request that the Examiner withdraw the objection and grant claims of the subject application a priority of U.S. Patent Application 09/376,276 and German Patent Application No. 198.37.438.0.

Confidential

## BEST AVAILABLE COPY

APPLICANT(S): GAZIT, Dan et al.  
SERIAL NO.: 10/067,980  
FILED: February 8, 2002  
Page 8

P-4891-US1

### CLAIM REJECTIONS-35 U.S.C. § 112, FIRST PARAGRAPH

In the Office Action, the Examiner rejected claims 23-29 and 42-47 under 35 U.S.C. § 112, first paragraph, as allegedly failing to convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of a method of repairing or forming a cartilage in a subject in need by administering any engineered cell expressing any factor of the T-box family to the subject at any site; and a composition comprising any engineered cell which expresses any factor of the T-box family and a pharmaceutically acceptable carrier."

The Examiner admitted, however, that the specification is enabling for a method of repairing or forming a cartilage in a subject in need, comprising the steps of (a) obtaining a mesenchymal stem cell from the subject; (b) transfecting the cell with a recombinant vector comprising a nucleic acid sequence encoding Brachyury, so as to obtain an engineered mesenchymal stem cell which expresses Brachyury; and (c) administering the engineered mesenchymal stem cell to a site of cartilage damage in the subject, thereby repairing or forming a cartilage in the subject; and is also enabling for a composition comprising an engineered mesenchymal stem cell which expresses Brachyury and a pharmaceutically acceptable carrier.

In response, without conceding the correctness of the Examiner's assertion, Applicants have herein amended claims 23-29 to be directed to a method of repairing or forming a cartilage in a subject in need comprising the steps of (a) obtaining a mesenchymal stem cell from the subject; (b) transfecting the mesenchymal stem cell with a recombinant vector comprising a nucleic acid sequence encoding a Brachyury protein, so as to obtain an engineered cell which expresses a Brachyury protein; and (c) administering the engineered cell to the subject at a site of cartilage damage in the subject, thereby repairing or forming cartilage in a subject in need; and have amended claims 42-47 to be directed to a composition

Confidential

## BEST AVAILABLE COPY

APPLICANT(S): GAZIT, Dan et al.  
SERIAL NO.: 10/067,980  
FILED: February 8, 2002  
Page 9

P-4891-US1

comprising an engineered mesenchymal stem cell which expresses a Brachyury protein and a pharmaceutically acceptable carrier.

Accordingly, Applicants respectfully request withdrawal of the rejection.

### CLAIM REJECTIONS-35 U.S.C. § 112, SECOND PARAGRAPH

In the Office Action, the Examiner rejected claims 23-29 under 35 U.S.C. § 112, second paragraph, alleging that there is no linkage in claims 23-29 between the recited steps with the preamble "repairing or forming a cartilage" of the claims.

In response, Applicants have amended independent claim 23 to include the language "thereby repairing or forming cartilage in a subject." Applicants respectfully assert that the claims as amended herein comply with the Examiner's rejection, and accordingly request withdrawal of the rejection.

### 35 U.S.C. § 101 REJECTIONS

In the Office Action, the Examiner provisionally rejected claims 23-29 and 42-47 under the judicially created doctrine of statutory type (35 U.S.C. § 101) double patenting as being unpatentable over claims 23-29 and 43-48 of copending Application No. 10/298215.

Section 804 of the Manual of Patent Examining Procedure states that "If the provisional double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent."

Confidential

## BEST AVAILABLE COPY

APPLICANT(S): GAZIT, Dan et al.  
SERIAL NO.: 10/067,980  
FILED: February 8, 2002  
Page 10

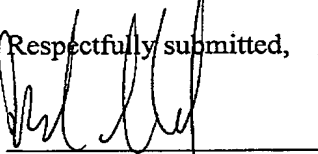
P-4891-US1

Since all of the other objections and rejections of the Examiner have been addressed, Applicants respectfully request that the Examiner withdraw the statutory type double patenting rejection in accordance with Section 804 of the Manual of Patent Examining Procedure and allow claims 23-29 and 42-47.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to Deposit Account No. 05-0649.

Respectfully submitted,



Mark S. Cohen  
Attorney for Applicant(s)  
Registration No. 42,425

Dated: June 24, 2004

**Eitan, Pearl, Latzer & Cohen Zedek, LLP.**  
10 Rockefeller Plaza, Suite 1001  
New York, New York 10020  
Tel: (212) 632-3480  
Fax: (212) 632-3489

Confidential